REMARKS

Applicants respectfully request entry of amendments to claims 1, 22, and 38. Support for the amendments can be found throughout the specification, including paragraphs [0009], [0012], [0020], [0060], [0065], [0067], [0068], [0072], [0076], [0078], [0099], [0130], [0134], [0152]; Example 8; and the originally filed claims and, therefore, do not add new matter. Further, Applicants submit that the Office Action is incomplete as claims 34-38 recited in the Amendment of June 12, 2006, were neither addressed nor entered, and the Action is silent with respect to the disposition of these claims. As such, Applicants respectfully request that the finality with respect to prosecution of the instant application be withdrawn.

Applicants submit that pending claims 1, 9-13, 15, 16, 22-32, and 34-38 are in condition for allowance, or are in better condition for presentation on appeal, and respectfully request that the claims as amended be entered.

Rejections Under 35 U.S.C. §103

Claims 1, 9-13, 15, and 16 stand rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Hogan in view of Shamblott et al.

Applicants traverse the rejection as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First there must be some suggestion or motivation in the references themselves or in knowledge generally available to one of skill in the art, to modify the reference or combine the reference teachings. Second, there must be a reasonable expectation of success. And, finally the prior art reference (or references when combined) must teach all claim limitations. The teaching or suggestion and reasonable expectation of success must both be found in the prior art and not in Applicants' disclosure. (See M.P.E.P. §706.02(j)).

Applicants submit that because the cited references do not teach disaggregated single cells that upon dissociation from embryoid bodies can adhere to a defined substrate lacking a feeder layer or that such single cells have the ability to be maintained in culture on the defined substrate in the absence of a feeder layer or that such single undifferentiated cells lack

telomerase activity, the references when combined do not teach the invention as claimed. Thus, one of skill in the art would not be motivated to combine the reference teachings.

The Office Action alleges, in pertinent part, that Hogan teaches: a) cells of similar morphology/physiology as claimed produced from mouse primordial cells (citing col. 6, ll. 19-49); b) that such cells are selected in a similar fashion as claimed (citing col. 8, ll. 5-9); c) that human equivalents are taught (citing col. 5, ll. 3-5 and col. 9, ll. 18-11[sic]), including methods of using such cells (citing col. 5, ll. 32-34); d) that mouse "EBD-cells" undergo at least 20 population doublings" (citing col. 8, ll. 14-16); and e) that Hogan teaches that LIF may or may not be required for the maintenance of ES cells (citing col. 4, ll. 55-67). The Action then provides Shamblott et al. to support the position that such cells undergo "at least 30 or at least 60 population doublings, proliferate under conditions nonpermissive for the proliferation of human EG cells. Proliferate under conditions lacking LIF, a fibroblast feeder layer, or both, and transfectable with a retrovirus, lentivirus, or both." However, review of Hogan demonstrates that the reference does not teach the elements as recited in the amended claims, including maintenance of such cells in the absence of a feeder layer. For example, the referenced citations of the Action teach a) that the "rounded colonies of densely packed ES-like cells were carefully picked up with a finely drawn pipet . . . before seeding into wells containing feeder cells" (emphasis added) (col. 6, ll. 19-49); b) "[f]or further subculture, individual colonies of cells . . . were replated on a fresh feeder layer with added factors" (emphasis added) (col. 8, ll. 5-9); c) "[i]n later passages, these cultures were transferred to feeder layers of STO cells in medium without added factors . . . for a total of at least 20 passages" (emphasis added) (col. 8, ll. 11-16, inclusive). And further, while Hogan may or may not teach that "LIF make[sic] not be required for the maintenance of ES cells," nothing in Hogan teaches or suggests that the cells can be maintained in the absence of a feeder layer (see, especially, FIG. 1 and legend).

Moreover, the deficiency identified in the primary reference is not cured by Shamblott et al. For example, Shamblott et al. explicitly recite that:

> "Generation and passage of derived cultures were less successful when mouse embryo fibroblasts, human fetal fibrobalsts, or gelatin coated tissue culture dishes were substituted for STO cells, or when hrLIF or hrbFGF were withdrawn."

Shamblott et al., Proc Natl Acad Sci USA (1998) 95:13726-13731, at 13729, col. 1, first full paragraph.

Accordingly, Applicants submit that, in fact, Hogan and Shamblott et al. "teach away" from the present invention because one of skill in the art would only extract that when feeder cells are substituted, or when factors are withdrawn, efficacious maintenance of cells does not occur (e.g., after 6 days, which would be less than 20 doublings, in the presence of feeder cells alone, almost no ES cells remain; see, Hogan, FIG. 1A- 1C, open circles). Further, that Hogan in view of Shamblott et al. teach cells that undergo at least 30 or at least 60 population doublings finds no support in either reference. At best, Hogan only supports 20 passages (e.g., see Abstract and through out the document) and Shamblott et al. supports at most 25 (see, e.g., p. 13730, col. 1, first paragraph), and neither 20 nor 25 is at least 30. Moreover, it is well known in the art that the PGC related cells as described by Hogan and Shamblott et al. possess telomerase activity (see, e.g., Donovan and Gearhart, Nature (2001) 414:92-97, at Table 1; Exhibit A), an activity which is absent in the EBD cells of the present invention as claimed (see, e.g., Example 8 of the instant disclosure).

Again, the "teaching or suggestion **and** reasonable expectation of success must **both** be found in the prior art." (Emphasis added). One cannot simple use the Applicants' disclosure as a "blueprint" to reconstruct, by hindsight, Applicants' claim. See, e.g., Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 227 U.S.P.Q. 543 (Fed. Cir. 1985). Because there is neither the suggestion nor expectation of success that can be found in the cited art, no *prima facie* case of obviousness has been established.

Applicants submit that because there is no reasonable expectation of successfully achieving the invention as claimed, there is no motivation to combine the cited references, thus, no *prima facie* case for obviousness exists. For these reasons, Applicants respectfully request that the rejection, including as it might be applied against the amended claims, be withdrawn.

Claims 22-24, 27, and 30-32 stand rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Hogan in view of Shamblott et al.

Applicants traverse the rejection as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

As stated above, the properties of the present cells would not be obvious in view of the biochemical (e.g., lack of telomerase activity) and physiological (e.g., can be maintained in the absence of a feeder layer) differences between the EBD cells of the present invention and those cells as described in Hogan and Shamblott et al. The Office Action alleges that a method of obtaining such cells is obvious in view of the cited references. While Applicants submit that such an allegation may support an obvious to try (in hindsight) rationale, obvious to try is not the standard under § 103. "The admonition that 'obvious-to-try' is not the standard under § 103 has been directed mainly at two kinds of error"

i) "In some cases, what would have been 'obvious-to-try' would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of the many possible choices is likely to be successful."

ii) "In others, what was 'obvious-to-try' was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it." In re O'Farrell, 853 F.2d 894, 7 U.S.P.Q.2d 1673, 1681 (Fed. Cir. 1988). Applicants submit that the Action has committed an error of the second kind. As the biochemical and physiological properties of the EBD cells of the present invention could not be expected from the combined teachings of the cited references, at best, they provide only a general guidance for obtaining undifferentiated ES cells from germ cells, not the undifferentiated EBD cells of the present invention.

Again, the "teaching or suggestion **and** reasonable expectation of success must **both** be found in the prior art." (Emphasis added). One cannot simple use the Applicants' disclosure as a "blueprint" to reconstruct, by hindsight, Applicants' claim. See, e.g., Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 227 U.S.P.Q. 543 (Fed. Cir. 1985). Because there is neither the suggestion nor expectation of success that can be found in the cited art, no *prima facie* case of obviousness has been established.

Applicants submit that because there is no reasonable expectation of successfully achieving the invention as claimed, there is no motivation to combine the cited references, thus,

no *prima facie* case for obviousness exists. For these reasons, Applicants respectfully request that the rejection, including as it might be applied against the amended claims, be withdrawn.

Claims 22 and 27-29 stand rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Hogan in view of Shamblott et al, further in view of Rohwedel et al.

Applicants traverse the rejection as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

As stated above, the properties of the present cells would not be obvious in view of the biochemical (e.g., lack of telomerase activity) and physiological (e.g., can be maintained in the absence of a feeder layer) differences between the EBD cells of the present invention and those cells as described in Hogan and Shamblott et al. Further, because the biochemical and physiological properties of the EBD cells of the present invention could not be expected from the combined teachings of the Hogan and Shamblott et al., at best, they provide only a general guidance for obtaining cells ES cells from germ cells, not the undifferentiated EBD cells as presently claimed. Further, the Rohwedel et al. reference does not teach or suggest the elements as recited in the present claims. Thus, because there is no suggestion or expectation of success regarding obtaining EBD cells with the properties as claimed in view of the primary references, whether Rohwedel et al. teach or do not teach culturing of mouse EB cells on tissue culture plates coated with gelatin is immaterial.

Applicants submit that because there is no reasonable expectation of successfully achieving the invention as claimed, there is no motivation to combine the cited references, thus, no *prima facie* case for obviousness exists. For these reasons, Applicants respectfully request that the rejection, including as it might be applied against the amended claims, be withdrawn.

Conclusion

Applicants submit that pending claims 1, 9-13, 15, 16, 22-32, and 34-38 are in condition for allowance, or are in better condition for appeal. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this submission.

A check in the amount of $120.00 is enclosed to cover a One Month Petition for Extension of Time fee. No additional fee is deemed necessary with the filing of this paper. However, the Commissioner is hereby authorized to charge any additional fees required by this submission, or credit any overpayments, to Deposit Account No. 07-1896 referencing the above-identified docket number. A duplicate copy the Transmittal Sheet is enclosed.

Respectfully submitted,

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Daryl A. Basham, J.D., Ph.D.
Registration No. 45,869
Telephone: (858) 677-1429
Facsimile: (858) 677-1465

DLA Piper US LLP
4365 Executive Drive, Suite 1100
San Diego, California 92121-2133
USPTO Customer Number 28213